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EXAMINER	
TRAN, MY CHAU T	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 02/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,590	JURGENSEN ET AL.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-60* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/02/2005 has been entered.

Application and Claims Status

2. Applicant's preliminary amendment and response filed 11/02/2005 is acknowledged and entered. Claim 39 has been amended.

3. The amendment filed on 02/16/2005: amended claims 39, 40, and 60.

4. The amendment filed on 09/02/2004 and 09/03/2004: amended claims 39, 40, 44-50, and 54-60.

5. The amendment filed on 07/21/2004: cancelled claims 1-38 and added claims 39-60.

6. The amendment filed on 07/18/2003: cancelled claims 4, 6, 10-12, and 23; amended claims 1, 7, 13, 15, 18, 19, and 31; and added claims 37 and 38.

7. The amendment filed on 12/30/2002: cancelled claims 23 and 32 and amended claims 1, 5-7, 19, 21, and 31.

8. Claims 39-60 are pending.

9. Claims 39-60 are under consideration in this Office Action.

10. *The instant claimed invention recite a method of separating at least one target component from a biological sample.*

The method comprises the steps of a) placing the biological sample into a separation container; b) centrifuging the separation container containing the biological sample to densitometrically separate components of the biological sample into layers such that separation of the first set of selection microbeads and the second set of selection microbeads is induced and the elongated target layer is located within the focusing device of the separation container; and c) aspirating the elongated target layer to remove at least one target component from the separation container.

The separation container comprises 1) a focusing device, 2) a first set of selection microbeads, and 3) a second set of selection microbeads.

The first set of selection microbeads having at least one target affinity binding agent bound to their surfaces and the target affinity binding agent bind to the target component within the biological sample, which refers to the limitation of "at least one target affinity binding agent having binding affinity for at least one target component within the biological sample".

The second set of selection microbeads having different density than the first set of selection microbeads and having at least one different affinity binding agent bound to their surfaces. The different affinity binding agent has a binding affinity for a component other than the target component within the biological sample.

The focusing device has a specific density substantially equal to the density of the first set of selection microbeads, an axial bore passage and being capable of vertical movement within the separation container upon centrifugation. The limitation that the focusing device has a specific density substantially equal to the density of the first set of selection microbeads, an axial bore passage is interpreted as that the focusing device has a specific density substantially equal to the density of the first set of selection microbeads and has a structure of an axial bore passage.

Claim Objections

11. Claim 43 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In this case if the limitation that "*said focusing device having a specific density substantially equal to the density of the first set of selection microbeads, an axial bore passage*" of claim 39 is amended to recite that the instant claimed focusing device have a specific density equal the instant claimed first set of selection microbeads and has a structure of the instant claimed axial bore passage than claim 43 fail to further limit the instant claimed focusing device of the previous (independent) claim 39.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 39-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 39 recite the limitation that "*said focusing device having a specific density substantially equal to the density of the first set of selection microbeads, an axial bore passage*" is vague and indefinite because it unclear whether the limitation is that the instant claimed focusing device have a specific density equal to both the instant claimed first set of selection microbeads and the instant claimed axial bore passage or that the

instant claimed focusing device have a specific density equal the instant claimed first set of selection microbeads and has a structure of the instant claimed axial bore passage. Thus, this limitation is vague and indefinite and claim 39 and all dependent claims are rejected under 35 USC 112, second paragraph.

b. Claim 39 recite the term "substantially" to further limit the term "equal" in the limitation that the instant claimed focusing device '*having a specific density equal to the density of the first set of selection microbeads, an axial bore passage*'. The term "substantially" is a relative term, which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also MPEP § 2173.05(b). Thus, claim 39 is indefinite and/or unclear and claim 39 and all dependent claims are rejected under 35 USC 112, second paragraph.

c. Claim 51 recites the limitation "said container" in line 1. There is insufficient antecedent basis for this limitation in the claim 39. Claim 39 recite " a separation container" and "said separation container" in line 3. Thus, claim 51 and all dependent claims are rejected under 35 USC 112, second paragraph.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 39-43, 47-49, 51-53, and 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. (US Patent 5,776,710; which is refers to as Levine '710) and Levine et al. (US Patent 5,393,674; which is refers to as Levine '674). *Note: This rejection has been modified to more clearly address applicants' newly amended claims and/or newly amended arguments.*

Levine '710 discloses the method for detecting a target analyte in a biological sample in a tube (see e.g. Abstract; col. 2, lines 35-64; claims 1-2). The method comprises the step of a) adding a group of density marker to the sample in a tube wherein the density marker have a predetermined specific gravity, and each density marker in the group are coupled with a binding material to form density marker couples wherein the binding material is specific to the target analyte; b) adding to the sample in a tube the labeled antibodies or other binding material to label all density markers which have target analyte bonded thereto; c) incubating the density marker and labeled binding material in the tube; d) centrifuging the sample so as to densimetrically separate the into a distinct location in the tube; and e) determining if any band exhibits the presence of the labeled binding material and therefore the presence of the target analyte (see e.g. col. 3, lines 10-65; col. 6, lines 21-29; col. 7, lines 34-57; claims 1 and 2). The tube comprises one or more bodies or group of bodies such as inserts or plastic beads of different densities that are coupled with capture binding material such as antibodies (see e.g. col. 2, lines 43-49; col. 3, lines 10-15, and 33-37). The different density beads can be differentially colored, i.e. one density from another, so that each differently colored band will designate a different target analyte (see e.g. col. 4, lines 9-32; col. 6, lines 21-29). Additionally, the tube contain a

cylindrical float or insert which maybe freely movable in the tube and has a specific gravity such that it come to rest in an area where the particles (density markers) also come to rest, i.e. bands of captured analytes coupled with binding material of the density markers will settle into the restricted space between the float/insert of the tube (see e.g. col. 2, lines 43-64; col. 4, lines 9-32; col. 6, lines 21-29).

The method of Levine '710 differs from the presently claimed invention by failing to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device.

Levine '674 disclose a method for harvesting target cells from centrifuged sample of blood contained in a tube which also contains a cylindrical float having a through passage for receiving and elongating layers of blood cell components to be harvested from the sample, the float having an axial constant outer diameter which ensures that the float fits snugly in the tube (see e.g. claim 1; fig. 1 and 4). The method steps of centrifuging the blood, tube, and float at sufficient G forces to move the float toward one end of the tube and forcing the blood cell components to settle in said through passage (see e.g. claim 1; fig. 1 and 4). The cells and components of the buffy coat layer are expanded linearly in the narrow bore channel in the float and thus can be easily harvested (see e.g. col. 3, lines 13-15). The method includes harvesting the target cells from the float bore (ref. #7 of fig. 5) with a needle (see e.g. col. 4, lines 55-57; fig. 5). Additionally, it is noted that figures 1 and 4 of Levine '674 are identical to figures 1 and 2 of the instant specification.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the step of removing the desired component and a ribbed such

that one or more axial passages exist in the focusing device as taught by Levine '674 in the method of Levine '710. One of ordinary skill in the art would have been motivated to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device in the method of Levine '710 for the advantage of providing a ten fold expansion of the white cell and platelet layers when performing the cell harvesting with the tube-float combination (Levine '674: col. 2, lines 50-60) since both Levine '710 and Levine '674 disclose the method of cell separation by density gradient centrifugation (Levine '710: col. 2, lines 35-64; Levine '674: col. 1, lines 7-14; fig. 1 and fig. 4). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Levine '710 and Levine '674 because Levine '674 claimed the method for harvesting target cells from centrifuged sample contained in a tube which also contains a cylindrical float having a through passage for receiving and elongating layers of components to be harvested from the sample (Levine '674: claim 1 and 2).

Therefore, the combine teachings of Levine '710 and Levine '674 do render the invention of the instant claims *prima facie* obvious.

16. Claims 44-46 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. (US Patent 5,776,710; which is refers to as Levine '710) and Levine et al. (US Patent 5,393,674; which is refers to as Levine '674) as applied to claims 39-43, 47-49, 51-53, and 57-59 above, and further in view of Dorn (US Patent 4,927,749).

The combine teachings of Levine '710 and Levine '674 are obvious over the presently claimed invention, i.e. the method of separating at least one target component from a biological sample.

Levine '710 discloses the method for detecting a target analyte in a biological sample in a tube (see e.g. Abstract; col. 2, lines 35-64; claims 1-2). The method comprises the step of a) adding a group of density marker to the sample in a tube wherein the density marker have a predetermined specific gravity, and each density marker in the group are coupled with a binding material to form density marker couples wherein the binding material is specific to the target analyte; b) adding to the sample in a tube the labeled antibodies or other binding material to label all density markers which have target analyte bonded thereto; c) incubating the density marker and labeled binding material in the tube; d) centrifuging the sample so as to densimetrically separate the into a distinct location in the tube; and e) determining if any band exhibits the presence of the labeled binding material and therefore the presence of the target analyte (see e.g. col. 3, lines 10-65; col. 6, lines 21-29; col. 7, lines 34-57; claims 1 and 2). The tube comprises one or more bodies or group of bodies such as inserts or plastic beads of different densities that are coupled with capture binding material such as antibodies (see e.g. col. 2, lines 43-49; col. 3, lines 10-15, and 33-37). The different density beads can be differentially colored, i.e. one density from another, so that each differently colored band will designate a different target analyte (see e.g. col. 4, lines 9-32; col. 6, lines 21-29). Additionally, the tube contain a cylindrical float or insert which maybe freely movable in the tube and has a specific gravity such that it come to rest in an area where the particles (density markers) also come to rest, i.e. bands of captured analytes coupled with binding material of the density markers will settle into the

restricted space between the float/insert of the tube (see e.g. col. 2, lines 43-64; col. 4, lines 9-32; col. 6, lines 21-29).

Levine '674 disclose a method for harvesting target cells from centrifuged sample of blood contained in a tube which also contains a cylindrical float having a through passage for receiving and elongating layers of blood cell components to be harvested from the sample, the float having an axial constant outer diameter which ensures that the float fits snugly in the tube (see e.g. claim 1; fig. 1 and 4). The method steps of centrifuging the blood, tube, and float at sufficient G forces to move the float toward one end of the tube and forcing the blood cell components to settle in said through passage (see e.g. claim 1; fig. 1 and 4). The cells and components of the buffy coat layer are expanded linearly in the narrow bore channel in the float and thus can be easily harvested (see e.g. col. 3, lines 13-15). The method includes harvesting the target cells from the float bore (ref. #7 of fig. 5) with a needle (see e.g. col. 4, lines 55-57; fig. 5). Additionally, it is noted that figures 1 and 4 of Levine '674 are identical to figures 1 and 2 of the instant specification.

Thus, the combine teachings of Levine '710 and Levine '674 are obvious over the presently claimed invention since one of ordinary skill in the art at the time the invention was made to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device as taught by Levine '674 in the method of Levine '710 as discussed fully in paragraph 15 above. However, the combine teachings of Levine '710 and Levine '674 differs from the presently claimed invention by failing to disclose microbeads having density of between 1.00 g/cc and about 1.06 g/cc.

Dorn discloses compositions and method of cell separation in biological specimens such as blood based upon the cells buoyant density (see e.g. Abstract; col. 1, lines 5-14; col. 4, line 62 thru col. 5, line 3; col. 5, lines 49-66). The compositions comprise colloidal silica particles with varying densities wherein the density ranges from 1.046 g/cm^3 to 1.43 g/cm^3 (see e.g. col. 7, line 64 thru col. 8, line 2; col. 8, Table 1) and the coupled with a reagent such as antibody (see e.g. col. 5, lines 25-39; col. 8, lines 21-30; col. 11, lines 24-62). Additionally, Dorn discloses the method of separating lymphocytes cells from blood sample with the composition having buoyant density of 1.060-1.074 g/cm^3 and B and T lymphocytes cells from blood sample (see e.g. col. 5, lines 62 thru col. 6, line 2; col. 6, lines 36-56; col. 17, lines 36-61; col. 18, lines 16-36).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose microbeads having density of between 1.00 g/cc and about 1.06 g/cc as taught by Dorn in the method of Levine '710 and Levine '674. One of ordinary skill in the art would have been motivated to disclose microbeads having density of between 1.00 g/cc and about 1.06 g/cc in the method of Levine '710 and Levine '674 for the advantage of providing a separation technique wherein the cell separation is accomplished by the movement of the peripheral blood cells during centrifugation to their respective buoyant densities within the continuous density gradient (Dorn: col. 4, lines 54-57) since Levine '710, Levine '674, and Dorn disclose the method of cell separation based on the cell buoyant densities (Levine '710: col. 2, lines 35-64; Levine '674: col. 1, lines 7-14; Dorn: col. 5, lines 49-62). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Levine '710, Levine '674, and Dorn because Dorn discloses by examples the success of

separating lymphocytes cells from blood sample using density colloidal silica particles (Dorn: col. 17, lines 36-61; col. 18, lines 16-36).

Therefore, the combine teachings of Levine '710, Levine '674, and Dorn do render the invention of the instant claims *prima facie* obvious.

17. Claims 50 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. (US Patent 5,776,710; which is refers to as Levine '710) and Levine et al. (US Patent 5,393,674; which is refers to as Levine '674) as applied to claims 39-43, 47-49, 51-53, and 57-59 above, and further in view of Van Vlasselaer (US Patent 5,646,004).

The combine teachings of Levine '710 and Levine '674 are obvious over the presently claimed invention, i.e. the method of separating at least one target component from a biological sample.

Levine '710 discloses the method for detecting a target analyte in a biological sample in a tube (see e.g. Abstract; col. 2, lines 35-64; claims 1-2). The method comprises the step of a) adding a group of density marker to the sample in a tube wherein the density marker have a predetermined specific gravity, and each density marker in the group are coupled with a binding material to form density marker couples wherein the binding material is specific to the target analyte; b) adding to the sample in a tube the labeled antibodies or other binding material to label all density markers which have target analyte bonded thereto; c) incubating the density marker and labeled binding material in the tube; d) centrifuging the sample so as to densimetrically separate the into a distinct location in the tube; and e) determining if any band exhibits the presence of the labeled binding material and therefore the presence of the target analyte (see e.g.

col. 3, lines 10-65; col. 6, lines 21-29; col. 7, lines 34-57; claims 1 and 2). The tube comprises one or more bodies or group of bodies such as inserts or plastic beads of different densities that are coupled with capture binding material such as antibodies (see e.g. col. 2, lines 43-49; col. 3, lines 10-15, and 33-37). The different density beads can be differentially colored, i.e. one density from another, so that each differently colored band will designate a different target analyte (see e.g. col. 4, lines 9-32; col. 6, lines 21-29). Additionally, the tube contain a cylindrical float or insert which maybe freely movable in the tube and has a specific gravity such that it come to rest in an area where the particles (density markers) also come to rest, i.e. bands of captured analytes coupled with binding material of the density markers will settle into the restricted space between the float/insert of the tube (see e.g. col. 2, lines 43-64; col. 4, lines 9-32; col. 6, lines 21-29).

Levine '674 disclose a method for harvesting target cells from centrifuged sample of blood contained in a tube which also contains a cylindrical float having a through passage for receiving and elongating layers of blood cell components to be harvested from the sample, the float having an axial constant outer diameter which ensures that the float fits snugly in the tube (see e.g. claim 1; fig. 1 and 4). The method steps of centrifuging the blood, tube, and float at sufficient G forces to move the float toward one end of the tube and forcing the blood cell components to settle in said through passage (see e.g. claim 1; fig. 1 and 4). The cells and components of the buffy coat layer are expanded linearly in the narrow bore channel in the float and thus can be easily harvested (see e.g. col. 3, lines 13-15). The method includes harvesting the target cells from the float bore (ref. #7 of fig. 5) with a needle (see e.g. col. 4, lines 55-57;

fig. 5). Additionally, it is noted that figures 1 and 4 of Levine '674 are identical to figures 1 and 2 of the instant specification.

Thus, the combine teachings of Levine '710 and Levine '674 are obvious over the presently claimed invention since one of ordinary skill in the art at the time the invention was made to include the step of removing the desired component and a ribbed such that one or more axial passages exist in the focusing device as taught by Levine '674 in the method of Levine '710 as discussed fully in paragraph 15 above. However, the combine teachings of Levine '710 and Levine '674 differs from the presently claimed invention by failing to disclose cells other than white blood cells such as fetal cells.

Van Vlasselaer disclose a method for density-adjusted cell sorting that uses cell type-specific binding agent such as antibodies linked to carrier particles to impart a different density to undesired cell populations allowing fetal cells to be separated during centrifugation (see e.g. Abstract; col. 1, lines 6-22; col. 2, lines 42-64). The method uses carrier particles with density of 1.0702 gr/ml, i.e. 1.0702 g/cm^3 (see e.g. col. 5, lines 16-48; col. 9, lines 13-63; col. 11, line 42 thru col. 13, line 3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to disclose cells other than white blood cells such as fetal cells as taught by Van Vlasselaer in the method of Levine '710 and Levine '674. One of ordinary skill in the art would have been motivated to disclose cells other than white blood cells such as fetal cells in the method of Levine '710 and Levine '674 for the advantage of providing a rapid and high yield isolation of fetal cells from maternal peripheral blood (Van Vlasselaer: col. 2, lines 29-41) since Levine '710, Levine '674, and Van Vlasselaer disclose the method of cell separation based on

the cell buoyant densities (Levine '710: col. 2, lines 35-64; Levine '674: col. 1, lines 7-14; Van Vlasselaer: col. 2, lines 42-64). Furthermore, one of ordinary skill in the art would have a reasonable expectation of success in the combination of Levine '710, Levine '674, and Van Vlasselaer because Van Vlasselaer discloses by examples the success of separating fetal cells from maternal blood cells (Van Vlasselaer: col. 12, line 19 thru col. 13, line 3).

Therefore, the combine teachings of Levine '710, Levine '674, and Van Vlasselaer do render the invention of the instant claims *prima facie* obvious.

Withdrawn Rejection(s)

18. The rejections of claims 39-60 under 35 USC 112, second paragraph, as being indefinite regarding the phrase "substantially absent" in claim 39 has been withdrawn in light of applicant's amendments of claim 39 wherein applicant has cancelled the limitation of "*and wherein said second set of selection microbeads and said components other than said at least one target component of said biological sample are substantially absent from said axial bore passage of said focusing device after centrifugation*", which include the phrase "substantially absent".

Response to Arguments

19. Applicant's arguments directed to the rejection under 35 USC 103(a) as being unpatentable over Levine et al. (US Patent 5,776,710; which is refers to as Levine '710) and Levine et al. (US Patent 5,393,674; which is refers to as Levine '674) were considered but they are not persuasive for the following reasons. *Note: This rejection has been modified to more clearly address applicants' newly amended claims and/or newly amended arguments.*

Applicant contends that the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is not obvious over the presently claimed method because 1) "*the analyte-binding material is affixed to a solid surface is at least one reason why Levine '710 failed to teach or even suggest removal of the analyte*", i.e. the analyte is immobile; 2) "*Levine '674 does not teach, mention or even suggest that microbeads or particulate carriers be used in conjunction with the float.*"; 3) there is no motivation and /or expectation of success for the combination of the references. Therefore, the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is not obvious over the presently claimed method.

Applicant's arguments are not convincing since the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is obvious over the presently claimed method.

First, in response to applicant's argument that "*the analyte-binding material is affixed to a solid surface is at least one reason why Levine '710 failed to teach or even suggest removal of the analyte*", i.e. the analyte is immobile is contradictory to the instant claimed invention wherein the analyte is bound to the microbeads, i.e. instant claim 39 recites the limitation that '*the first set of selection microbeads having at least one target affinity binding agent bound to their surfaces and the target affinity binding agent bind to the target component within the biological sample, which refers to the limitation of "at least one target affinity binding agent having binding affinity for at least one target component within the biological sample"*'.

Second, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based

on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, the presently claimed method would result is trapping and immobilizing the analyte, i.e. "*wherein a target layer comprising the first set of selection microbeads bound to at least one target component is located within the axial bore passage of the focusing device*" see claimed step (b), lines 2-5.

Third, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is found in the teaching of Levine '674, i.e. the advantage of providing a ten fold expansion of the white cell and platelet layers when performing the cell harvesting with the tube-float combination (Levine '674: col. 2, lines 50-60).

Fourth, in response to applicant's argument that there is no reasonable expectation of success to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is a reasonable expectation of success, i.e. obviousness does not require absolute predictability, however, at least some degree of predictability is required. (See MPEP 2143.02). In this case, there is some degree of predictability in the combine the teaching of

Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) since both disclose 'trapping' the analyte within the cylindrical plastic float or insert (Levine '710: col. 2, lines 35-64; Levine '674: col. 1, lines 7-14; fig. 1 and fig. 4). Thus, there is some degree of predictability in the combine the teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674).

Thus, the combine teaching of Levine et al. (which is refers to as Levine '710) and Levine et al. (which is refers to as Levine '674) is obvious over the presently claimed method, and the rejection is maintained.

Conclusion

20. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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mct
February 6, 2006

PADMASHRI PONNALURI
PRIMARY EXAMINER